The adaptive immune response to bacterial infection - focus on *Staphylococcus aureus*

Hiddensee, 27th of October, 2015

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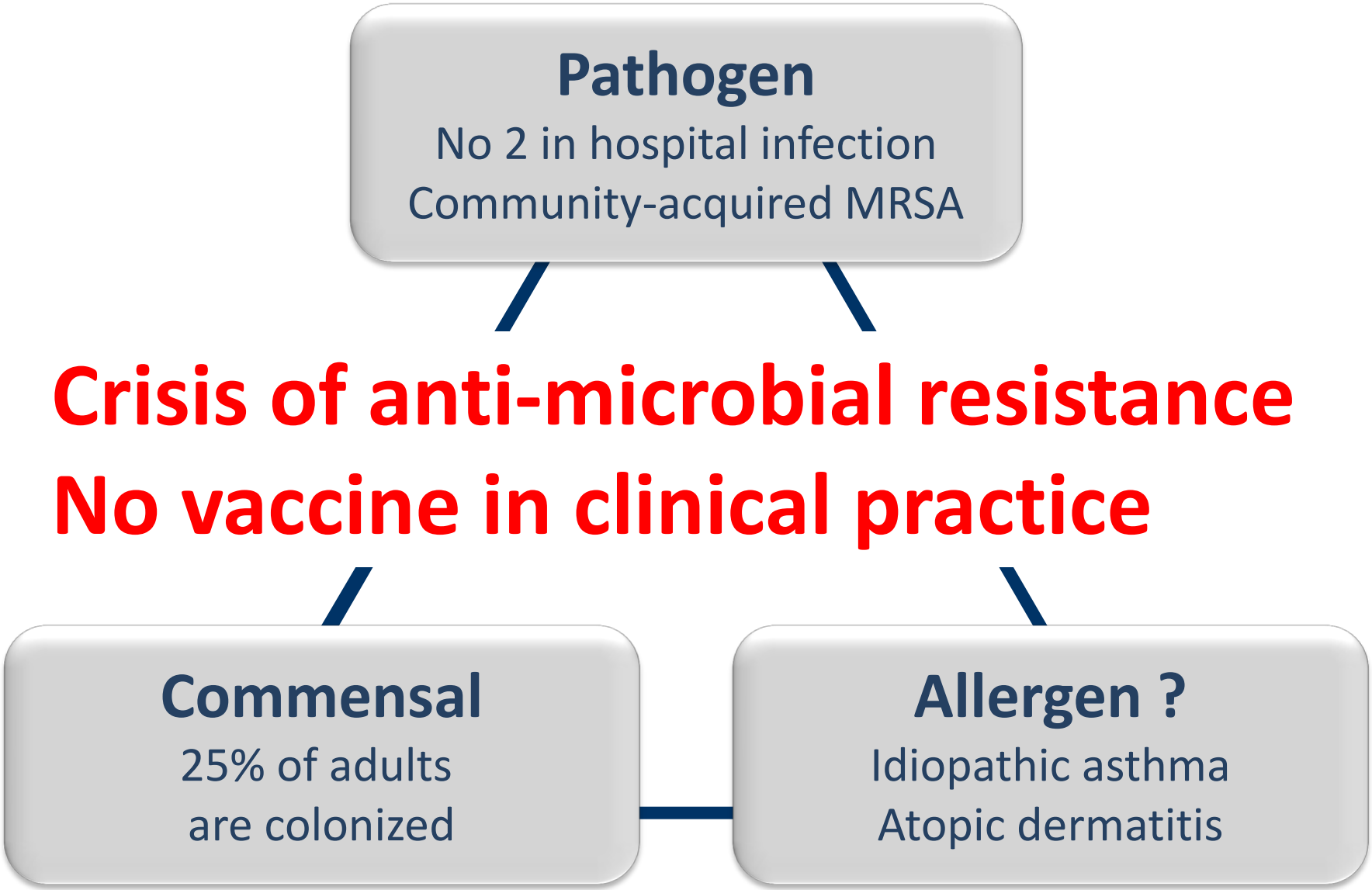
The many faces of *Staphylococcus aureus*



The leading question

Vaccination relies on immune memory,

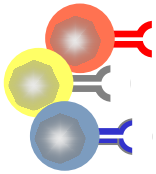
a core competence of the adaptive immune system.

What does the adaptive immune system contribute to the control of *S. aureus*?

Dimensions of the topic - methods

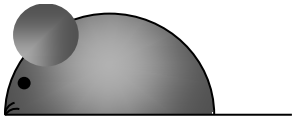
Targeted approach → **Unbiased approach**

Molecules



Cells

Cellular interactions



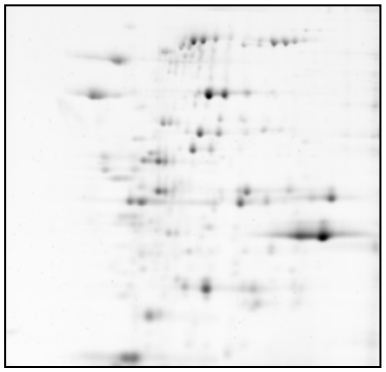
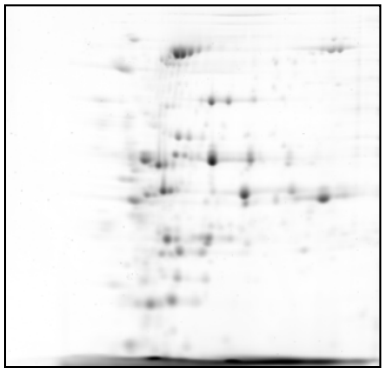
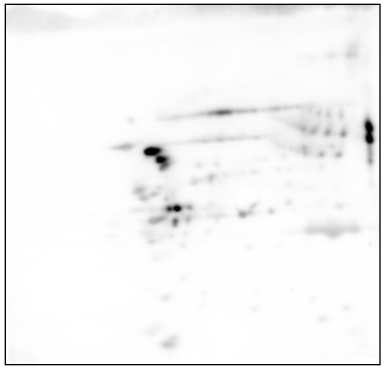
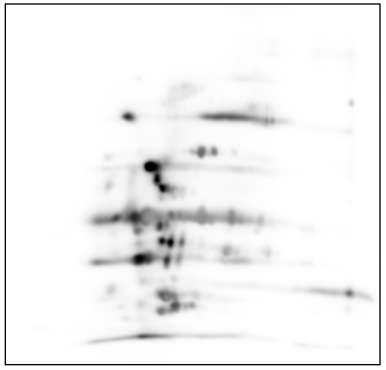
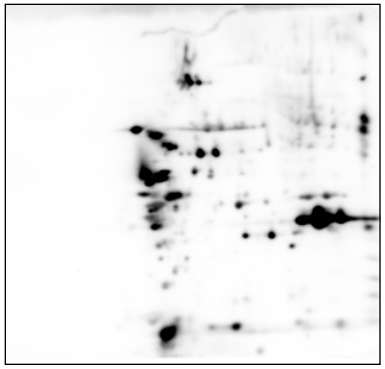
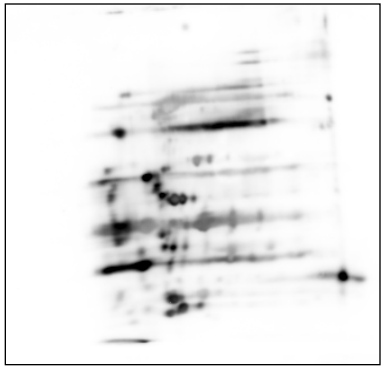
Animal models

Humans

Populations

What antigens are recognized?

➡Study the human natural immune response to *S. aureus*.

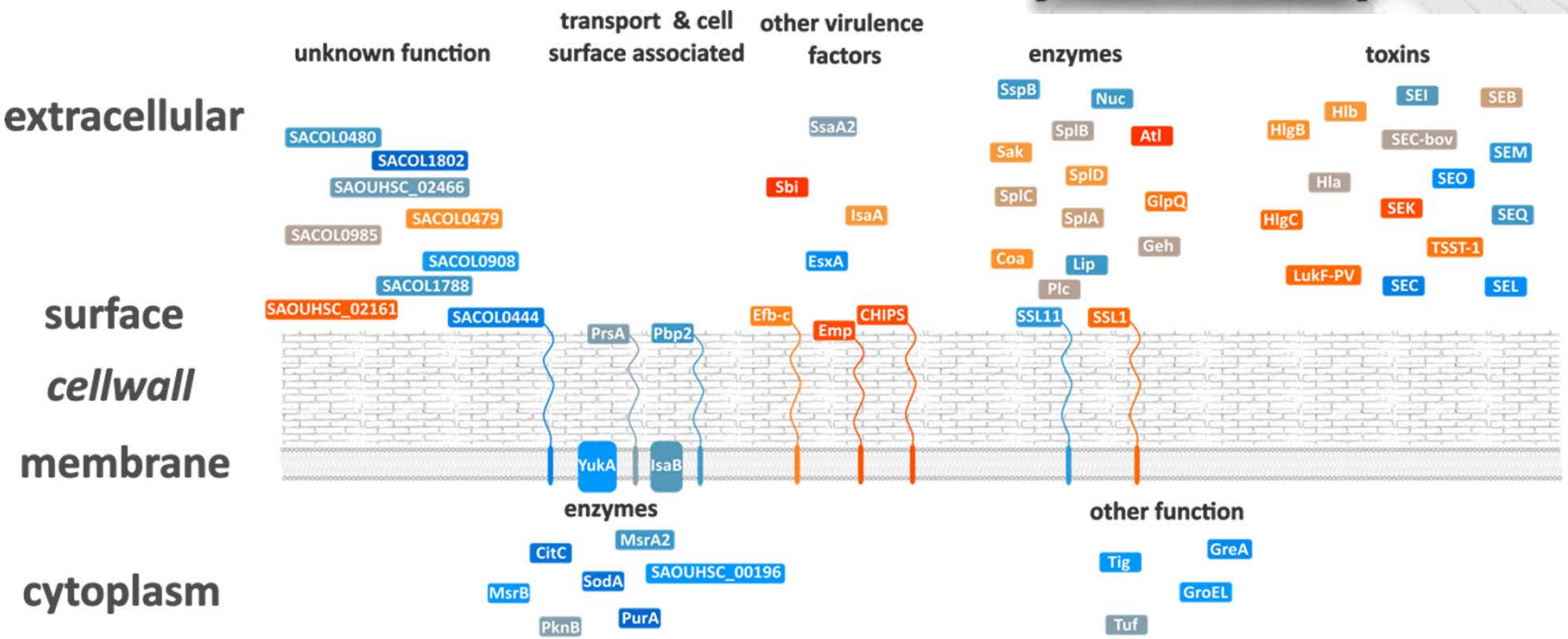
	Patient 1 (non-carrier) exogenous infection	Patient 2 (carrier) endogenous infection
bacterial proteins		
IgG before infection		
IgG during infection		

Kolata, Proteomics 2011

Measuring anti-*S. aureus* antibodies

Flexmap3D

Quantification of IgG binding to
> 100 recombinant *S. aureus* proteins

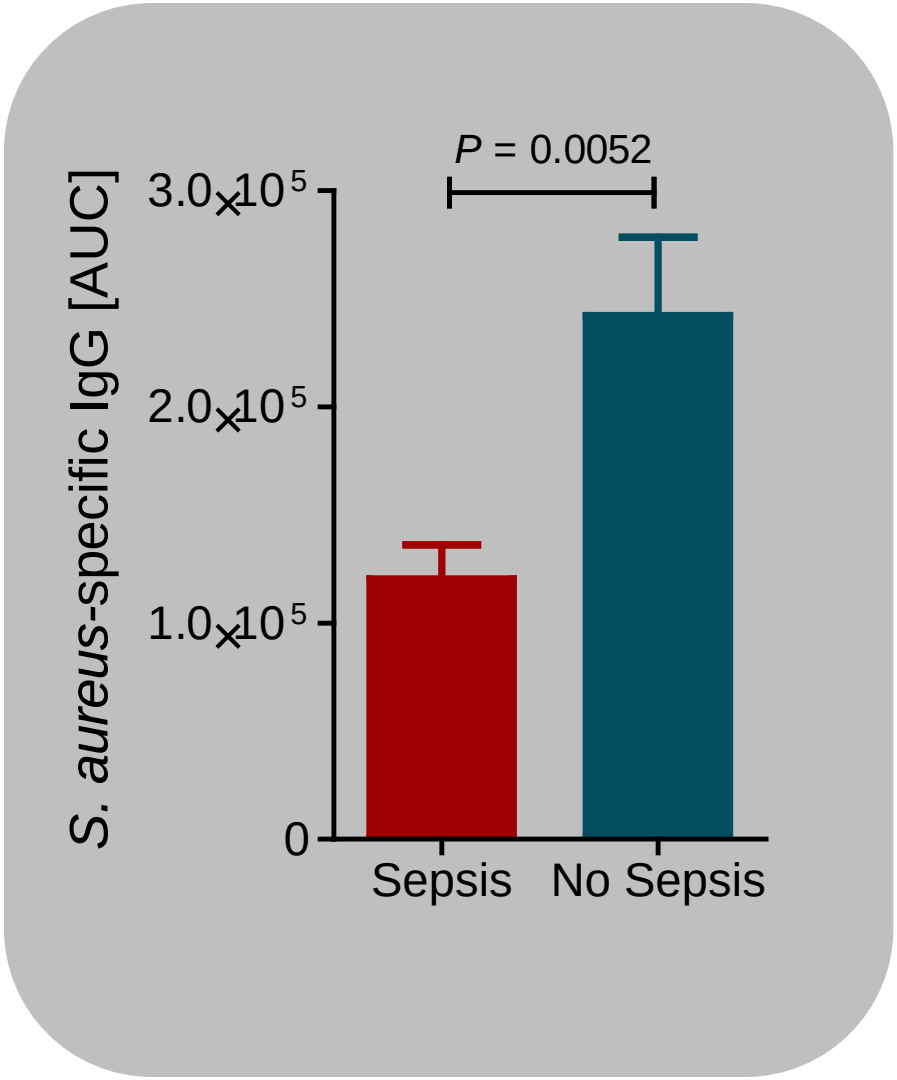


Collaboration: U. Völker, F. Schmidt, M.-C. Roughmann

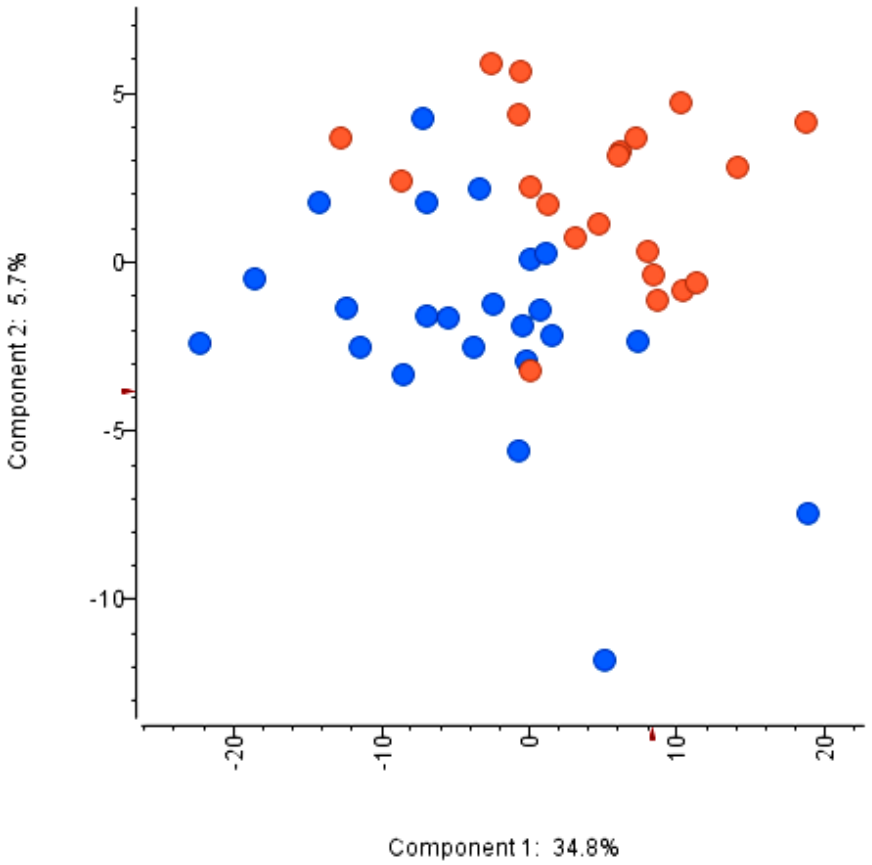
http://photos.labwrench.com/equipmentPhotos/3000/3048-3471.jpg

Stentzel et al., J. Proteomics 2015

More specific antibodies - less severe disease



Patient stratification in *S. aureus* blood stream infection



- Partial least square analysis (PLS)
- Ab binding to 8 *S. aureus* proteins

➡ correct prediction in 75%

no sepsis (n = 23)

sepsis (n = 21)

Collaboration: U. Völker, F. Schmidt, M.-C. Roughmann

Stentzel et al., J. Proteomics 2015

Mechanism of protection?

Antibodies

- neutralize virulence factors,
- opsonize bacteria,
- are biomarkers of immune memory.

Mechanisms of protection?

Hypothesis

The broad and specific antibody response implies a large pool of ***S. aureus* specific memory T cells**.

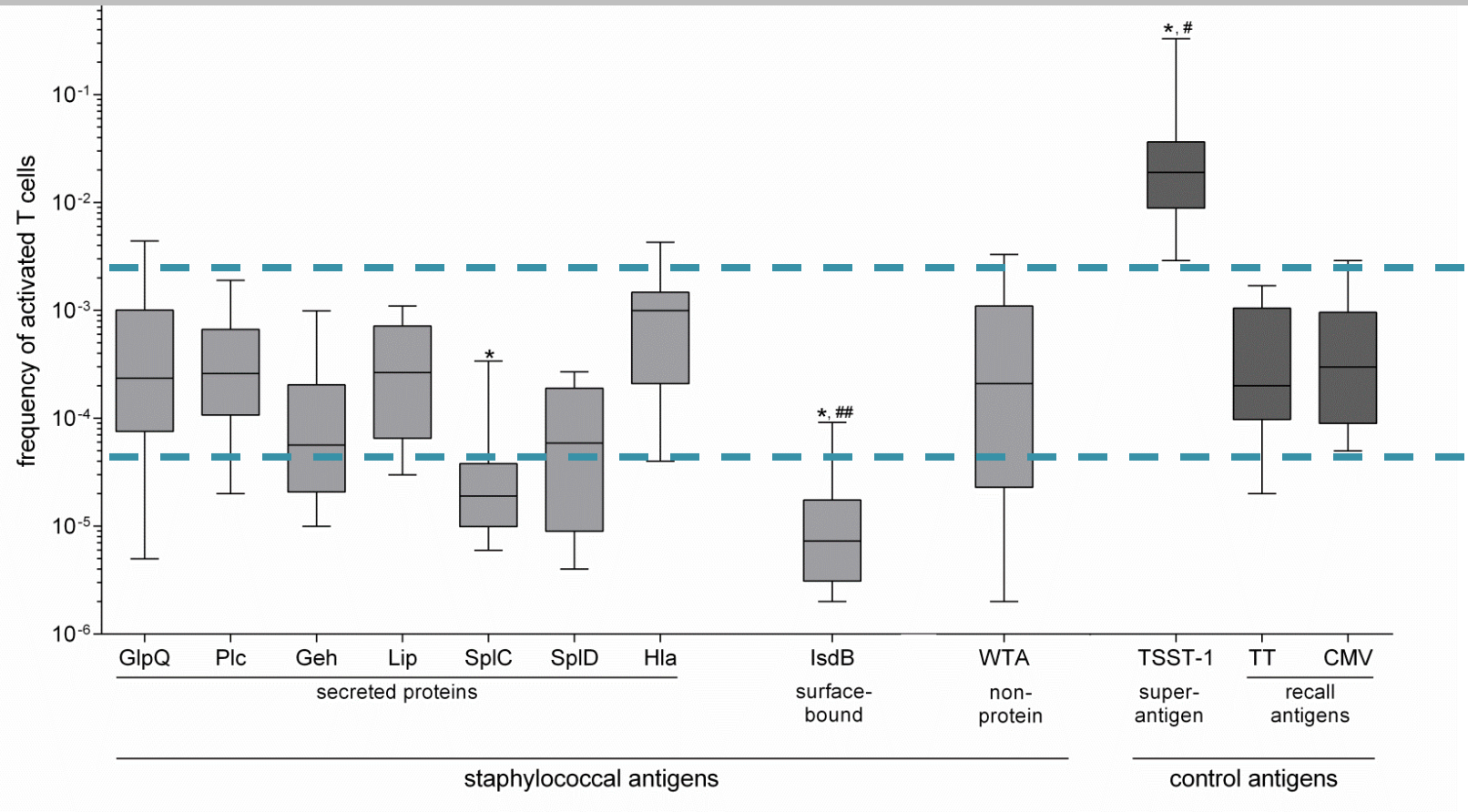
These strongly influence the course of a *S. aureus* infection.

How many *S. aureus*-reactive T cells?

What are they doing?

Robust human T cell response to *S. aureus* in human adults

3.6% of peripheral T cells recognize *S. aureus* with 35-fold differences between individuals (range 0.2-5.7%).



Kolata et al., JID 2015

Summary

S. aureus **elicits strong T- and B cell memory in humans**
➡ high cost of *S. aureus* control.

The adaptive immune system confers clinical protection during *S. aureus* invasion, but no sterile immunity.

***S. aureus*-mediated immune pathology?**